

INTERNATIONAL SEARCH REPORT

Int'l
Application No
PCT/GB2004/000198

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D487/04 A61P31/00 A61P35/00 A61K31/40 C07H3/02
//(C07D487/04, 209:00, 209:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BELL A A ET AL: "Synthesis of Casuarines 'Pentahydroxylated Pyrrolizidines' by Sodium Hydrogen Telluride-Induced Cyclisations of Azidodimesylates" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 38, no. 33, 18 August 1997 (1997-08-18), pages 5869-5872, XP004085896 ISSN: 0040-4039 p. 5869, introductory paragraph Cpds. 1-6,14,19,23,27</p> <p>-----</p> <p>-/-</p>	1-44

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

30 August 2004

Date of mailing of the International search report

07/09/2004

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WORMALD M R ET AL: "Configurational and conformational analysis of highly oxygenated pyrrolizidines: definitive identification of some naturally occurring 7a-epi-alexines" TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 9, no. 14, 17 July 1998 (1998-07-17), pages 2549-2558, XP004131419 ISSN: 0957-4166 p. 2549, last par. - p. 2550, first par. cpd. 2</p> <p>-----</p> <p>NASH ET AL.: "Casuarine: A very Highly Oxygenated Pyrrolizidine Alkaloid" TETRAHEDRON LETTERS, vol. 35, no. 42, 1994, pages 7849-7852, XP002274756 Cpd. 1; introductory paragraph page 7849</p> <p>-----</p> <p>DENMARK ET AL.: "Synthesis of (+)-Casuarine" ORGANIC LETTERS, vol. 1, no. 8, 1999, pages 1311-1314, XP002274757 Introductory paragraph; cpd. (1) page 1311</p> <p>-----</p> <p>DENMARK ET AL.: "Synthesis of (+)-Casuarine" J. ORG. CHEM., vol. 62, 2000, pages 2875-2886, XP002274758 Left column; cpd. (6) page 2875</p> <p>-----</p> <p>WORMALD M R ET AL.: "Casuarine-6-alpha-D-Glucoside from Casuarina Equisetifolia and Eugenia Jambolana" CARBOHYDRATE LETTERS, vol. 2, no. 3, 1996, pages 169-174, XP009028337 ISSN: 1073-5070 Introductory paragraph; cpds. 1, 2</p> <p>-----</p>	1-44
X		1-44

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national application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: -

It is not clear, how the expression the "derivative thereof" which is used in claims 1-2, 16-22 has to be understood. In a narrower interpretation it could be understood as one or more of the OH-hydrogens replaced by any chemically reasonable group.

Support within the meaning of Article 5 PCT is - in this case - to be found, however, for only a very small proportion of the compounds claimed, and the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

In a broader sense of the word "derivative" the product claims would also include compounds having a structural formula which is only similar to that as displayed in claim 1 (and it is again not clear where the line has to be drawn between similar molecules and those which are no longer within the scope the term "derivative"). The claims would - in this case - comprise a large number of known compounds such as alexine, australine or the epi-australines to name a few. This would lead to a very large number of documents relevant to the issue of novelty, and it would be impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, the compounds according to the structural formula in claim 1, pharmaceutically acceptable salts thereof and those derivatives in which one or more of the OH-hydrogens are substituted by an acyl group.

The above objections could be overcome by precising the term "derivative" as used in the claims, i.e. by substituting it by "acyl derivative".

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.